

Application No. 09/743,818  
Response to Office Action dated 08/19/2005  
February 17, 2006

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims:**

Claims 1-45. Canceled.

46 (Currently Amended). A method for reducing the susceptibility of tropoelastin to proteolysis comprising mutating an amino acid sequence of the tropoelastin which is susceptible to cleavage by one or more proteases selected from the group consisting of a serine protease and a metalloproteinase, so that the mutated amino acid sequence is not cleaved by the protease comprising mutating one or more amino acid residues corresponding to any of the following residues of SEQ ID NO:4:

- a) 1-12;
- b) 78-86;
- c) 81-89;
- d) 152-160;
- e) 441-451;
- f) 515-521;
- g) 564-574;

so that the susceptibility of tropoelastin to cleavage by a serine protease is reduced.

Claim 47. Cancelled.

48 (Previously Presented). A method according to claim 46 wherein one amino acid residue in the amino acid sequence is mutated.

49 (Currently Amended). A method according to claim 46 wherein the ~~protease is a~~ serine protease is serum protease, the method comprising mutating one or more amino acid residues corresponding to any of the following residues of SEQ ID NO:4:

- a) 1-12;
- b) 441-451;
- c) 515-521;
- d) 564-572;

so that the susceptibility of the tropoelastin to serum cleavage is reduced.

Claims 50 and 51. Cancelled.

52 (Currently Amended). A method according to claim 46 wherein the serine protease is plasmin, the method comprising mutating one or more amino acid residues corresponding to any of the following residues of SEQ ID NO:4:

- a) 1-8;
- b) 78-86;
- c) 81-89;

so that the susceptibility of the tropoelastin to plasmin cleavage is reduced.

Claim 53. Cancelled.

54 (Currently Amended). A method according to claim 46 wherein the serine protease is thrombin, the method comprising mutating one or more amino acid residues corresponding to any of the following residues of SEQ ID NO:4:

- a) 1-9;

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b) 152-160;

c) 515-521;

so that the susceptibility of the tropoelastin to thrombin cleavage is reduced.

Claims 55 and 56. Cancelled.

57 (Currently Amended). A method according to claim 46 wherein the protease is kallikrein, the method comprising mutating one or more amino acid residues corresponding to any of the following residues of SEQ ID NO:4:

a) 1-9;

b) 515-521;

c) 564-574;

so that the susceptibility of the tropoelastin to kallikrein cleavage is reduced.

Claims 58 - 89. Cancelled.

90 (New). A method according to claim 46, wherein the serine protease is serum protease, the method comprising mutating one or more amino acid residues corresponding to any of the following residues of SEQ ID NO:4:

a) 1-12;

b) 441-451;

c) 515-521;

d) 564-572;

so that the susceptibility of the tropoelastin to serum cleavage is reduced.

91 (New). A method according to claim 46, wherein the serine protease is trypsin, the method comprising mutating one or more amino acid residues corresponding to any of the residues 1-9 of SEQ ID NO:4 so that the susceptibility of the tropoelastin to trypsin cleavage is reduced.

92 (New). A method according to claim 46, wherein one amino acid residue is mutated.

93 (New). A method according claim 46, wherein the arginine residue corresponding to 515 of SEQ ID NO:4 is replaced with alanine.

94 (New). A method according to claim 46, wherein the serine protease is kallikrein, the method comprising mutating any of the residues corresponding to 515-521 of SEQ ID NO: 4 so that the susceptibility of the tropoelastin to kallikrein cleavage is reduced.

95 (New). A method according to claim 46, wherein the serine protease is trypsin, thrombin, kallikrein, plasmin and serum, the method comprising mutating one or more amino acid residues corresponding to any of residues 1 to 8 of SEQ ID NO: 4 so that the susceptibility of the tropoelastin to trypsin, thrombin, kallikrein, plasmin and serum is reduced.

96 (New). A method according to claim 46, wherein the serine protease is thrombin, kallikrein and serum, comprising mutating one or more amino acid residues corresponding to any of residues 1 to 8 or 515-521 of SEQ ID NO: 4 so that the susceptibility of the tropoelastin to kallikrein, thrombin and serum cleavage is reduced.

97 (New). A tropoelastin derivative produced by the method of claim 46.

98 (New). A method of reducing the susceptibility of tropoelastin to thrombin cleavage comprising mutating one or more amino acid residues corresponding to any of the following residues of SEQ ID NO:4:

- a) 1-9;
- b) 152-160;
- c) 515-521;

so that the susceptibility of the tropoelastin to thrombin cleavage is reduced.

99 (New). A method of reducing the susceptibility of tropoelastin to kallikrein cleavage comprising mutating one or more amino acid residues corresponding to any of the following residues of SEQ ID NO:4:

- a) 1-9;
- b) 15-521;
- c) 564-574;

so that the susceptibility of the tropoelastin to kallikrein cleavage is reduced.

100 (New). A method of reducing the susceptibility of tropoelastin to plasmin cleavage comprising mutating one or more amino acid residues corresponding to any of the following residues of SEQ ID NO:4:

- a) 1-8;
- b) 78-86;
- c) 81-89;

so that the susceptibility of the tropoelastin to plasmin cleavage is reduced.

101 (New). A method of reducing the susceptibility of tropoelastin to serum cleavage comprising mutating one or more amino acid residues corresponding to any of the following residues of SEQ ID NO:4:

- a) 1-12;
- b) 441-451;
- c) 515-521;
- d) 564-572;

so that the susceptibility of the tropoelastin to serum cleavage is reduced.

102 (New). A method of reducing the susceptibility of tropoelastin to trypsin cleavage comprising mutating one or more amino acid residues corresponding to any of the residues 1-9 of SEQ ID NO:4 so that the susceptibility of the tropoelastin to trypsin cleavage is reduced.

103 (New). A method according to claim 98, 99, 100 or 101, wherein one amino acid residue is mutated.

104 (New). A method according to claim 98, 99 or 101, wherein the arginine residue corresponding to 515 of SEQ ID NO:4 is replaced with alanine.

105 (New). A method of reducing the susceptibility of tropoelastin to kallikrein cleavage comprising mutating any of the residue 515-521 of SEQ ID NO: 4 so that the susceptibility of the tropoelastin to kallikrein cleavage is reduced.

106 (New). A method of reducing the susceptibility of tropoelastin to cleavage by trypsin, thrombin, kallikrein, plasmin and serum, comprising mutating one or more amino acid residues corresponding to any of residues 1 to 8 of SEQ ID NO: 4 so that the susceptibility of the tropoelastin to trypsin, thrombin, kallikrein, plasmin and serum is reduced.

107 (New). A method of reducing the susceptibility of tropoelastin to cleavage by thrombin, kallikrein, and serum, comprising mutating one or more amino acid residues corresponding to any of residues 1 to 8 or 515-521 of SEQ ID NO: 4 so that the susceptibility of the tropoelastin to kallikrein, thrombin and serum cleavage is reduced.

108 (New). A tropoelastin derivative produced by the method of claim 98, 99, 100 or 101.

109 (New). A method of reducing susceptibility of tropoelastin to cleavage by a metalloproteinase comprising mutating one or more amino acid residues corresponding to any of the residues 593-605 of SEQ ID NO:4 so that susceptibility of tropoelastin to cleavage by a metalloproteinase is reduced.

110 (New). A method according to claim 109, wherein the metalloproteinase is gelatinase B.

111 (New). A method of reducing the susceptibility of tropoelastin to gelatinase B cleavage comprising mutating one or more amino acid residues corresponding to any of the residues 593-605 of SEQ ID NO:4 so that the susceptibility of the tropoelastin to gelatinase B cleavage is reduced.

112 (New). A method according to claim 98 wherein the alanine at any one of residues 593, 595, 596 or 597 of SEQ ID NO:4 is replaced with another amino acid.

113 (New). A method according to claim 112, wherein the alanine corresponding to residue 593 of SEQ ID NO:4 is replaced with another amino acid.

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114 (New). A method according to claim 46, 98, 99, 100, 101, or 109, wherein the tropoelastin is human tropoelastin.